

Confirm. No. 4710  
516745-2001.1**REMARKS**

Reconsideration and withdrawal of the restriction/election of species and rejections of this application and consideration and entry of this paper are respectfully requested in view of the herein remarks, which place the application in condition for allowance.

**I. STATUS OF CLAIMS AND FORMAL MATTERS**

Claims 1-5, 7-22, and 24-26 are still pending in this application. Claim 11 was amended to correct a typographical error. The duplicate listing was not intended, but instead was meant to disclose a pair of compounds, one directed to 5,7-dihydroxy substitution and another to 5,7-dimethoxy substitution on the chromen-4-one moiety. Examples of this type of pairing can be seen through the compounds cited in claim 11. Claims 18 and 19 have been amended to correct the spelling of the term "hystiolytic" to ---histiocytic--- and delete the duplicate mention of "breast cancer". No new matter has been added.

Please also note that the certificate of facsimile transmission for the amendment filed on 3 February 2006 erroneously referred to the year "2005".

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited in the Office Action, and that these claims were in full compliance with the requirements of 35 U.S.C. § 112. The amendments of the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§§§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled.

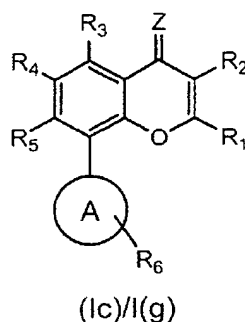
**II. TRAVERSAL OF RESTRICTION/ELECTION OF SPECIES REQUIREMENT**

Note for examiner: The traversal is otherwise the same as the traversal presented in the 3 February 2006 response except as indicated by the strikethrough and underlined text.

1. The applicants traverse the restriction and election of species based on the grounds that the search for the basic core structure of the applicants' claimed compound is not unduly burdensome and that the entire invention can be examined without difficulty.

The structure of formulas (Ic) and (Ig) is reproduced below:

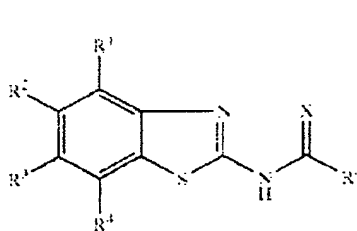
Confirm. No. 4710  
516745-2001.1



While at first glance the structure appears to be broad, several features simplify the search query. First, the variable Z is fixed to be oxygen or sulfur. Second, A is either a 5- or 6-membered heterocyclic ring which must be substituted with R<sub>6</sub> as defined in claim 1 or 5.

Based on the search conducted by the Examiner as published on Public PAIR and the references cited in the rejection below, no prior art was ever found which possessed all of these features of the applicants' claimed invention. Therefore, it is irrelevant as to whether additional heterocycles could be formed based on the definitions of the variables of the compound of formula (Ic) or (Ig) because the applicants compounds will always have the core structure of formula (Ic) or (Ig) with Z = O or S and A being a 5- or 6-membered heterocyclic ring which is substituted by R<sub>6</sub> as defined in ~~claims 1-5~~ claim 1 or 5, i.e. a core structure that yielded no hits during the Examiner's search for prior art.

There are numerous examples of compounds which encompass multiple heterocycles but were allowed because the core structure was novel and unobvious, e.g. see U.S. Patent 6,963,000 which was directed to a compound of formula (Ia):



the definition for R' includes numerous heterocyclic and non-heterocyclic moieties:

Confirm. No. 4710  
516745-2001.1

R<sup>1</sup> is phenyl, unsubstituted or substituted by halogen-lower alkyl, —C(O)H or by the following groups

—(CH<sub>2</sub>)<sub>n</sub>—C(O)—N(R<sup>5</sup>)—(CH<sub>2</sub>)<sub>m</sub>-lower alkoxy,  
—(CH<sub>2</sub>)<sub>n</sub>-O-halogen-lower alkyl,  
—(CH<sub>2</sub>)<sub>n</sub>-O—(CH<sub>2</sub>)<sub>m</sub>-O-lower alkyl,  
—S(O)<sub>2</sub>—N(R<sup>5</sup>)—(CH<sub>2</sub>)<sub>m</sub>-O-lower alkyl,  
—(CH<sub>2</sub>)<sub>n</sub>OR<sup>5</sup>,  
—(CH<sub>2</sub>)<sub>n</sub>N(R<sup>5</sup>)—(CH<sub>2</sub>)<sub>m</sub>-lower alkoxy,  
—(CH<sub>2</sub>)<sub>n</sub>N[(CH<sub>2</sub>)<sub>m</sub>-lower alkoxy]<sub>2</sub>,  
—(CH<sub>2</sub>)<sub>n</sub>N[S(O)<sub>2</sub>CH<sub>3</sub>]<sub>2</sub>,  
—(CH<sub>2</sub>)<sub>n</sub>N[R<sup>5</sup>][S(O)<sub>2</sub>CH<sub>3</sub>],  
—(CH<sub>2</sub>)<sub>n</sub>N(R<sup>5</sup>)-lower alkenyl,  
—(CH<sub>2</sub>)<sub>n</sub>N(R<sup>5</sup>)—(CH<sub>2</sub>)<sub>m</sub>-cycloalkyl,  
—(CH<sub>2</sub>)<sub>n</sub>N(R<sup>5</sup>)—C(O)O-lower alkyl,  
(CH<sub>2</sub>)<sub>n</sub>—S—(CH<sub>2</sub>)<sub>m</sub>—N(R<sup>5</sup>)(R<sup>6</sup>),  
—(CH<sub>2</sub>)<sub>n</sub>N(R<sup>5</sup>)—(CH<sub>2</sub>)<sub>m</sub>—S-lower alkyl,  
—(CH<sub>2</sub>)<sub>n</sub>N(R<sup>5</sup>)—S(O)<sub>2</sub>CH<sub>3</sub>,  
—(CH<sub>2</sub>)<sub>n</sub>N(R<sup>5</sup>)—(CH<sub>2</sub>)<sub>m</sub>-phenyl,  
—(CH<sub>2</sub>)<sub>n</sub>N(R<sup>5</sup>)—(CH<sub>2</sub>)<sub>m</sub>CH(OH)—CF<sub>3</sub>,  
—(CH<sub>2</sub>)<sub>n</sub>N(R<sup>5</sup>)—(CH<sub>2</sub>)<sub>m</sub>—CF<sub>3</sub>,  
—(CH<sub>2</sub>)<sub>n</sub>N(R<sup>5</sup>)—(CH<sub>2</sub>)<sub>m</sub>—O—CH(OH)—C<sub>6</sub>H<sub>5</sub>  
(OCH<sub>3</sub>)<sub>2</sub>,  
—(CH<sub>2</sub>)<sub>n</sub>N(R<sup>5</sup>)—(CH<sub>2</sub>)<sub>m</sub>—O—C(O)—C<sub>6</sub>H<sub>5</sub>(OCH<sub>3</sub>)<sub>2</sub>,  
—N(R<sup>5</sup>)—C(O)-morpholin,  
N(R<sup>5</sup>)—C(O)—N(R<sup>5</sup>)-phenyl, substituted by alkoxy,  
—S(O)<sub>2</sub>-morpholin,

or is phenyl, which is unsubstituted or substituted by —(CR<sup>5</sup>R<sup>6</sup>)<sub>n</sub>— five to seven membered aromatic or non aromatic heterocycle, and wherein the heterocycle is unsubstituted or substituted by hydroxy, —N(R<sup>5</sup>)(R<sup>6</sup>) or lower alkyl, or by —(CH<sub>2</sub>)<sub>n</sub>N(R<sup>5</sup>)(CH<sub>2</sub>)<sub>m</sub>— five or six membered aromatic or non aromatic heterocycle and wherein the heterocycle is unsubstituted or substituted by hydroxy, —N(R<sup>5</sup>)(R<sup>6</sup>) or lower alkyl,  
or is —N(R<sup>5</sup>)-phenyl, which is unsubstituted or substituted by lower alkoxy, or

Moreover, with the cancellation of -NR<sup>9</sup>R<sup>10</sup> possibly forming an additional heterocyclic ring the scope of the compounds is less than the scope of the compounds as originally filed (the applicants reserve the right to further prosecute the scope of the original claims in a continuing application).

With regard to the election of species requirement, while the possibility of additional heterocycles could cause cross-referencing in additional class/subclasses, the primary classification of the invention will be based on the structure represented by the structure of formula (Ic) and formula (Ig).

Confirm. No. 4710  
516745-2001.1

Therefore, the applicants claims do not constitute an undue burden on the Office and the restriction/election of species can be withdrawn because:

- (1) the chemical structure search of the applicants' claimed core structure did not yield any hits for prior art which is *prima facie* evidence of the lack of an undue burden; and/or
- (2) compounds with multiple recitations of heterocyclic rings have previously been examined and allowed; and/or
- (3) the present scope of the claims is narrower than that of the originally filed claims.

2. With regard to the restriction of the method of use and the method of making claims from the compound claims, the applicants request that these claims be rejoined upon allowance of the compound claims (see MPEP 821.04 - Rejoinder).

3. With regard to the assertion that certain compounds in claim 11 did not fall under the generic concept, it is noted that the compounds designated as "page 170, the last species" and "page 171, the first species" have been cancelled (These compounds correlate to (+/-)-*trans*-2-(2-Chloro-phenyl)-8-(2-imidazol-1-ylmethyl-1-methyl-pyrrolidin-3-yl)-5,7-dimethoxy-chromen-4-one; (+/-)-*trans*-2-(2-Chloro-phenyl)-5,7-dihydroxy-8-(2-imidazol-1-ylmethyl-1-methyl-pyrrolidin-3-yl)-chromen-4-one, respectively). These compounds represented certain embodiments of the invention where -NR<sub>9</sub>R<sub>10</sub> could form an additional heterocyclic ring. The applicants reserve the right to further pursue these compounds in a continuing application.

The compounds designated as "page 168, the 5<sup>th</sup> and 6<sup>th</sup> species" and "page 169, the 5<sup>th</sup> and 6<sup>th</sup> species" correspond respectively to:

- (+)-*trans*-8-(2-Hydroxymethyl-1-methyl-pyrrolidin-3-yl)-5,7-dimethoxy-2-thiophen-2-yl-chromen-4-one;
- (+)-*trans*-5,7-Dihydroxy-8-(2-hydroxymethyl-1-methyl-pyrrolidin-3-yl)-2-thiophen-2-yl-chromen-4-one;
- (+/-)-*trans*-2-(2-Chloro-pyridin-3-yl)-8-(2-hydroxymethyl-1-methyl-pyrrolidin-3-yl)-5,7-dimethoxy-chromen-4-one;
- (+/-)-*trans*-2-(2-Chloro-pyridin-3-yl)-5,7-dihydroxy-8-(2-hydroxymethyl-1-methyl-pyrrolidin-3-yl)-chromen-4-one.

Confirm. No. 4710  
516745-2011.1

These compounds have been maintained in claim 11 and represent certain embodiments of the invention wherein  $R_1$  may be a heterocyclic ring which is still encompassed by the pending claims. These compounds should be considered part of the examined invention because the search for these compounds do not represent an undue burden on the Office for the reasons cited in paragraph 1 above.

### CONCLUSION

In view of the remarks and amendments herewith, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date, and, the Examiner is invited to telephonically contact the undersigned to advance prosecution. The Commission is authorized to charge any fee occasioned by this paper, or credit any overpayment of such fees, to Deposit Account No. 50-0320.

Respectfully submitted,  
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